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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,444	10/24/2005	Dayuan Wang	58260-011600/US	4302

33717 7590 11/03/2006

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EXAMINER

RAHMANI, NILOOFAR

ART UNIT	PAPER NUMBER
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1625

DATE MAILED: 11/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/528,444	Applicant(s) WANG ET AL.	
	Examiner Niloofar Rahmani	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 September 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7, 10-14, 17-19, 22, 23, 29, 30 and 33-36 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 4-6, 12, 13, 29, 35 and 36 is/are allowed.
- 6) ☒ Claim(s) 1-3, 7, 10, 11, 14, 17-19, 22, 23, 30, 33 and 34 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 1-7, 10-14, 17-19, 22-23, 29-30, 33-36 are currently pending in the instant application. Claims 8-9, 15-16, 20-21, 24-28, 31-32 are cancelled.

Priority

2. This application is file on 10/24/2005, which is a 371 of PCT/CN03/00748, filed on 09/04/2003, which claims the priority of CHINA 021306869, filed on 09/18/2002.

3. The rejection of claims 7-11,14-18,19-28, and 30-34 under 35 U.S.C. 112, second paragraph for " the use if immunosuppressive agent or anti-inflammatory agent" is withdrawn in view of the applicant's amendment.

4. The rejection of claims 7-11,14-18,19-28, and 30-34 under 35 U.S.C. 101 because the claimed recitation of a use is withdrawn in view of the applicant's amendment.

5. The rejection of claims 2,4,6,13, and 35-36 under 35 U.S.C. 112, second paragraph for the term " a method for preparation of the compound" is withdrawn in view of the applicant's amendment.

6. The rejection of claims 7, 10-11, 14, 17-19, 22-23, 30, and 33-34 under 35 U.S.C. 112, first paragraph is maintained for reason of record. Applicants argue that Example 11 and Example 12 proved the effect for treatment of inflammatory disease of WDY compounds; Example 14 and Example 15 proved the effect for treatment of arthritis of WDY compounds; and Example 16 proved the effect for prevention of organ rejection of WDY compounds. It is the examiner's position

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that the specification, while being enabling for arthritis disease and heart transplanted with WDY6 and WDY7, does not reasonably provide enablement for treating any other claimed diseases. On page 16, and 18 of the specification, applicant has rat's models of arthritis diseases such as Dinitrochlorobenzene (DNCB) model and Cotton-ball model. On page 21, Table 6 and page 23, Table 8 of the specification, applicant disclosed the compounds WDY6, WDY7 using for treating arthritis diseases and heart transplanted.

7. Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rejected because the term "[[H,]]" is confusing. Is H out or is that in. Correction is required.

8. Claim 2 is rejected because " the first lead compound triptolide" has no antecedent basis in the base claim 1. Inclusion in claim 1 is recommended.

9. Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 7, 10-11, 14, 17-19, 22-23, 30, and 33-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating specific diseases, does not reasonably provide enablement for preventing diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Applicants are not enabled for preventing any of these diseases. The only established prophylactics are vaccines not the compounds such as present here. In addition, it is presumed that "prevention" of the claimed diseases would require a method of identifying those individuals who will develop the claimed diseases before they exhibit symptoms. There is no evidence of record that would guide the skilled clinician to identify those who have the potential of becoming afflicted.

"The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art, and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. 1) As discussed above, preventing diseases requires identifying those patients who will acquire the disease before *** occurs. This would require extensive and potentially opened ended clinical research on healthy subjects. 2) The passage spanning line 27, page 5 to line 6, page 6 lists

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the diseases Applicant intend to treat. 3) There is no working example of such a preventive procedure in man or animal in the specification. 4) The claims rejected are drawn to medical treatment and are therefore physiological in nature. 5) The state of the art is that no general procedure is art-recognized for determining which patients generally will become afflicted with disease before the fact. 6) The artisan using Applicants invention would be a Board Certified physician who specialized to treat diseases with an MD degree and several years of experience. Despite intensive efforts, pharmaceutical science has been unable to find a way of getting a compound to be effective for the prevention of inflammatory diseases generally. Under such circumstances, it is proper for the PTO to require evidence that such an unprecedented feat has actually been accomplished, *In re Ferens*, 163 USPQ 609. No such evidence has been presented in this case. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech vs. Novo Nordisk*, 42 USPQ2d 1001, 1006. This establishes that it is not reasonable to any agent to be able to prevent inflammatory diseases generally. That is, the skill is so low that no compound effective generally against inflammatory diseases has ever been found let alone one that can prevent such conditions. 7) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24

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(CCPA 1970). 8) The claims broadly read on all patients, not just those undergoing therapy for the claimed diseases and on the multitude of compounds embraced by Formula I, II, IIIa, and IIIb.

The Examiner suggests deletion of the word "prevention".

10. Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S.

1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 3 is rejected under 103(a) as being unpatentable over Wang et al., WO 00/63212.

Determination of the scope and content of the prior art (MPEP §2141.01)

Wang et al. disclosed the instant claimed compound on page 2-3, wherein R₁ being alkyl having 1-4 carbon atoms, -C(=O)(CH₂)_nCO₂, wherein n being 1-4 and R₂ being -SCN.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and the prior art compounds is that Wang et al. compounds have the possibility of 11 arrangements that R_1 can be. Four of those 11 possibilities encompassed by claim 3.

Finding of prima facie obviousness-rational and motivation (MPEP §2142.2143)

One having ordinary skill in the art would have been motivated to pick 4 of those 11 possibilities. Because picking 4 of 11 possibilities is within skill in the ordinary artisan.

11. Allowable Subject Matter

Claims 4-6, 12-13, 29, and 35-36 are patentable over Wang et al. WO 00/63212. The reference teaches six fused rings instead of the seven fused rings compounds of the instant application. Therefore, the claims are free of prior art. The method of treating arthritis would be seen as allowable over the prior art.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Niloofar Rahmani whose telephone number is 571-272-4329. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thomas Mckenzie, can be reached on 571-272-0670. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or public PAIR. Status information for unpublished applications is available through Private PAIR

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only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

NILOOFAR RAHMANI

10/24/2006

NR



MARGARET D. SEAMAN

PRIMARY EXAMINER

GROUP 1625

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